DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: DEC 17 2002

From: Consumer Safety Officer, Division of Standards and Labeling Regulations, Office of Nutritional Products, Labeling and Dietary Supplements, HFS-821

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

Subject of the Notification:	Hirudo powder
Firm:	Wealth Express Industrial Ltd.
Date Received by FDA:	March 11, 2002
90-Day Date:	June 9, 2002

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification and related correspondence for the aforementioned substance should be placed on public display in docket number 95S-0316 as soon possible since it is past the 90-day date. Thank you for your assistance.

Rhonda L. Kane

Rhonda R. Kane, M.S., R.D.

Attachments

95S-0316

RPT120

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD

MAY 24 2002

Mr. Shiming Han
Vice President
Wealth Express Industrial Ltd.
Block B1, 19/F Kailey Industrial Center
12 Fung Yip St. Chai Wan
Hong Kong

Dear Mr. Han:

This letter is in response to your notification, dated March 5, 2002, submitted to the Food and Drug Administration (FDA) for a new dietary ingredient pursuant to 21 U.S.C. 350b(a)(2) (section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act). FDA received your submission on March 11, 2002. Your letter notified FDA of your intent to market a product containing "Hirudo powder" that you assert is a new dietary ingredient. On July 9, 2001, you submitted a new dietary ingredient notification for the same ingredient. FDA responded to your first notification in a letter dated September 21, 2001, that the information provided in the submission did not provide an adequate basis to conclude that Hirudo powder, when used under the conditions recommended or suggested in the labeling of your product, would reasonably be expected to be safe.

Your submission states that you intend to market Hirudo powder as a dietary ingredient that constitutes 20% of a dietary supplement product called "Promoting Blood Circulation Capsule" (PBCC), manufactured by Siping Pharmaceutical Co., Ltd. In addition to Hirudo powder, PBCC consists of three other major components, namely "membranous milkvetch root, rehmannia dride rhizome, and king solomonseal rhizome". The levels of these three main ingredients are not disclosed in your submission, nor are any characterizations provided of that 80% portion of PBCC. Your submission states that PBCC was approved in 1995 by the State Drug Administration of China as a Class III new herbal medicine to be marketed as an over the counter drug. PBCC is marketed in 500mg capsules containing 100 mg Hirudo powder. The PBCC label recommends taking three capsules after each meal or nine capsules daily for a total daily intake of 900 mg Hirudo powder.

21 U.S.C. 350b(a)(2) requires that a manufacturer or distributor of a dietary supplement that contains a new dietary ingredient submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under 21 U.S.C 350b(a)(2), there must be a history of use or other evidence of safety establishing that the dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is deemed to be adulterated under 21 U.S.C. 342(f)(1)(B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

FDA has carefully evaluated the information in your submission. Your submission contains evidence of history of use of Hirudo powder as a medicine in China and other information that you assert is an adequate basis to conclude that a dietary supplement product containing Hirudo powder will reasonably expected to be safe. However, FDA has several significant concerns about the evidence on which you rely to support your conclusion.

First, PBCC is not a dietary supplement because it does not meet the statutory definition of a dietary supplement in that Hirudo powder is not a "dietary ingredient" as defined in 21 U.S.C. 321(ff). Hirudo powder is not a vitamin, mineral, herb or other botanical, amino acid, dietary substance for use by man to supplement the diet by increasing the total dietary intake, or a concentrate, metabolite, constituent, extract or combination of any ingredient described above. Hirudo powder cannot be viewed as part of man's usual food or drink. Therefore, PBCC is not a food or a dietary supplement.

Even if PBCC could meet the definition of a dietary supplement, FDA does not agree that the evidence on which you rely supports your conclusion that a dietary supplement containing Hirudo powder, when used under the conditions recommended or suggested in the labeling of your product, will reasonably expected to be safe. Your submission documents a history of medicinal use for Hirudo powder. No substantiation of the clinical safety of Hirudo powder is provided in your notification. To support your assertion of safety, you rely on inadequate evidence from several sources. First, you provide references to Hirudo powder's use as a traditional medicine in China. A long history of use of a medicinal substance in traditional therapies does not provide assurance of safety for a dietary supplement because the conditions of use are so different. Moreover, the Chinese literature that you supplied as exhibits in support of your notification suggests that Hirudo powder is toxic and that it is used for removal of blood stasis, among other indications, because of its anticoagulant properties.[1,2] Therefore, the history of use of this substance in traditional medicine provides inadequate assurance that Hirudo powder will reasonably expected to be safe when used under the conditions recommended or suggested in the labeling of a dietary supplement containing the substance. In addition, you provide acute and subchronic toxicity tests for PBCC in rodents. The extrapolation of the results of these tests to the use of Hirudo powder is inappropriate because the test product contains multiple substances, not Hirudo powder per se.

Finally, you assert in your notification that there are a lack of reports of adverse reactions associated with the use of PBCC as a medicine in China[3,4]. FDA is not aware of any systematic collection of data related to adverse effects occurring in individuals using PBCC. Further, absence of adverse event reports does not necessarily mean a particular product or ingredient has not been or is not likely to be associated with an adverse event, nor does it provide evidence of safety.

We also have concerns about the cautionary statement you propose to include as a condition of use for Hirudo powder. Throughout your submission, Hirudo powder's abortifacient properties are noted. However, the cautionary statement you propose to include as a condition of use for Hirudo powder that the ingredient should not be used by pregnant women does not address the risks for those in the earliest phases of pregnancy when a woman may not be aware she is pregnant.

In summary, for the reasons discussed above, PBCC is not a dietary supplement as defined in 21 U.S.C. 321(ff). Even if your product were a dietary supplement it would be adulterated under 21

---

[1] Exhibit 1: Pharmacopoeial Committee of the Ministry of Health, People's Republic of China, 1995. "Hirudo (Schuizhi)", Pharmacopoeia of the People's Republic of China, Part 1, p. 67

[2] Exhibit 3: Wong Weiliang, Fang Shuting, Oct. 1979, Drugs for Activating Blood Flow and Removing Blood Stasis, Section 3, *Hirudo nipponica* Whitman, Clinical Traditional Chinese Medicinal Science, pp. 936-940.

[3] Exhibit 4: Lan, Lin, December 25, 2001, "Specification of Promoting Blood Circulation Capsule", translation from Chinese

[4] Exhibit 5: Shushan, Cao, December 27, 2002 "About Promoting Blood Circulation Capsule", translation from Chinese

U.S.C. 342(f)(1)(B) as a dietary supplement that contains a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury. Furthermore, a product like yours that does not appear to be a dietary supplement or a food under the Act and that is represented to affect the structure or function of the body of man appears to be a drug within the meaning of 21 U.S.C. 321(g)(1)(C). As such, it is subject to regulation under the drug provisions of the Act. If you wish Hirudo powder to be evaluated as a drug, you should contact FDA's Center for Drug Evaluation and Research, Office of Compliance, HFD-310, 7520 Standish Place, Rockville, Maryland 20855.

Your submission will be kept confidential for 90 days from the date of receipt, and after June 9, 2002, your submission will be placed on public display at Dockets Management Branch (Docket No. 95S-0316). Commercial and confidential information in the notification will not be made available to the public.

Should you have any questions concerning this matter, please contact me at (301) 436-2371.

Sincerely yours,

Felicia B. Satchell

Felicia B. Satchell
Director
Division of Standards
and Labeling Regulations
Office of Nutritional Products, Labeling
and Dietary Supplements

Enclosures